Amendments to the Claims:

Please add claims 46-99. This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A method to produce an immunoglobulin with fully human variable region or an analog thereof, specific for a desired antigen, which method comprises:

administering said antigen or an immunogenic portion thereof to a nonhuman animal under conditions to stimulate an immune response, whereby said animal produces B cells that secrete immunoglobulin specific for said antigen; wherein said nonhuman animal is characterized by being substantially incapable of producing endogenous heavy or light immunoglobulin chain variable regions, but capable of producing human immunoglobulin variable regions; and

recovering said immunoglobulin or analog.

2. Canceled.

3. (Original) The method of claim 1 wherein said recovering step comprises immortalizing B cells from said animal, screening the resulting immortalized cells for the secretion of said immunoglobulin, and

1) recovering immunoglobulin secreted by said immortalized B cells, or

2) recovering the genes encoding at least the variable region of said immunoglobulin from the immortalized B cells, and optionally modifying said genes;

expressing said genes or modified forms thereof to produce immunoglobulin or analog; and

recovering said immunoglobulin or analog.

4. (Original) The method of claim 1 wherein said recovering step comprises

recovering genes encoding at least the variable region of immunoglobulins from the primary B cells of the animal;

generating a library of said genes expressing the variable regions;

screening the library for a variable region with desired affinity for the antigen;

recovering the genes encoding said variable regions;

expressing said recovered genes to produce an immunoglobulin or analog containing said variable region and recovering said immunoglobulin or analog.

5. (Original) A recombinant DNA molecule comprising a nucleotide sequence encoding the immunoglobulin or analog produced by the method of claim 1.

6. Canceled

7. (Previously Presented) A cell or cell line modified to contain the DNA molecule of claim 5.

8. (Original) A method to produce an immunoglobulin with fully human variable region or an analog thereof which method comprises culturing the cells of claim 7 under

conditions whereby said encoding nucleotide sequence is expressed to produce said immunoglobulin or analog; and recovering said immunoglobulin or analog.

9. (Original) A DNA molecule comprising a nucleotide sequence corresponding to the gene or modified gene prepared by the method of claim 3.

10. Canceled

11. (Original) A cell or cell line modified to contain the DNA molecule of claim 9.

12. (Previously Presented) A method to produce an immunoglobulin with fully human variable regions or an analog thereof which method comprises culturing the cells of claim 11 under conditions whereby said encoding nucleotide sequence is expressed to produce said immunoglobulin or analog; and recovering said immunoglobulin or analog.

13. (Original) A DNA molecule which comprises a nucleotide sequence encoding a variable region with desired affinity prepared according to the method of claim 4.

14. Canceled

15. (Original) A cell or cell line modified to contain the DNA molecule of claim 13.

16. (Previously Presented) A method to produce an immunoglobulin with fully human variable region or an analog thereof which method comprises culturing the cells of claim 15 under conditions whereby said encoding nucleotide sequence is expressed to produce said immunoglobulin or analog; and recovering said immunoglobulin or analog.

17. (Original) An immortalized B cell which secretes an immunoglobulin to a desired antigen with a fully human variable region prepared according to claim 3.

18. (Original) A method to produce an immunoglobulin or analog which comprises culturing the cells of claim 17 and recovering said immunoglobulin or analog.

19. (Original) An immunoglobulin with fully human variable region or analog produced by the method of claim 1.

20. (Original) The immunoglobulin or analog of claim 19 wherein the desired antigen is selected from the group consisting of

the leukocyte markers, CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a,b,c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27 and its ligand, CD28 and its ligands B7.1, B7.2, B7.3, CD29 and its ligand, CD30 and its ligand, CD40 and its ligand gp39, CD44, CD45 and isoforms, CDw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1 and TCR;

the histocompatibility antigens, MHC class I or II, the Lewis Y antigens, SLex, SLey, SLea, and SLeb;

the integrins, VLA-1, VLA-2, VLA-3, VLA-4, VLA-5, VLA-6, and LFA-1;

the adhesion molecules, Mac-1 and p150,95;

the selectins, L-selectin, P-selectin, and E-selectin and their counterreceptors VCAM-1, ICAM-1, ICAM-2, and LFA-3;

the interleukins, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-11, IL-12, IL-13, IL-14, and IL-15;

interleukin receptors, IL-1R, IL-2R, IL-4R, IL-5R, IL-6R, IL-7R, IL-8R, IL-10R, IL-11R, IL-12R, IL-13R, IL-14R, and IL-15R;

chemokines, PF4, RANTES, MIP1α, MCP1, NAP-2, Groα, Groβ, and IL-8;

growth factors, TNFalpha, TGFbeta, TSH, VEGF/VPF, PTHrP, EGF family, FGF, PDGF family, endothelin, and gastrin releasing peptide (GRP);

growth factor receptors, TNFalphaR, RGFbetaR, TSHR, VEGFR/VPFR, FGFR, EGFR, PTHrPR, PDGFR family, EPO-R, GCSF-R and other hematopoietic receptors;

interferon receptors, IFNαR, IFNβR, and IFNγR;

Igs and their receptors, IgE, FceRI, and FCeRII;

tumor antigens, her2-neu, mucin, CEA and endosialin;

the allergens, house dust mite antigen, lol p1 (grass) antigens, and urushiol;

the viral proteins, CMV glycoproteins B, H, and gCIII, HIV-1 envelope glycoproteins, RSV envelope glycoproteins, HSV envelope glycoproteins, EBV envelope glycoproteins, VZV envelope glycoproteins, HPV envelope glycoproteins, Hepatitis family surface antigens;

the toxins, pseudomonas endotoxin and osteopontin/uropontin, snake venom, and bee venom;

the blood factors, complement C3b, complement C5a, complement C5b-9, Rh factor, fibrinogen, fibrin, and myelin associated growth inhibitor;

the enzymes, cholesterol ester transfer protein, membrane bound matrix metalloproteases, and Glutamic acid decarboxylase (GAD); and

the miscellaneous antigens ganglioside GD3, ganglioside GM2, LMP1, LMP2, eosinophil major basic protein, eosinophil cationic protein, pANCA, Amadori protein, Type IV collagen, glycated lipids, γ-interferon, A7, P-glycoprotein and Fas (AFO-1) and oxidized-LDL.

21. (Previously Presented) A DNA molecule comprising a nucleotide sequence that encodes the immunoglobulin or analog of claim 19.

22. Canceled

23. (Previously Presented) A cell or cell line modified to contain the DNA molecule of claim 21.

24. (Original) A method to produce an immunoglobulin or analog specific for the antigen selected from the group consisting of leukocyte markers, CD2, CD3, CD4, CD5, CD6, CD7, CD8, CDlla,b,c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27 and its ligand, CD28 and its ligands B7.1, B7.2, B7.3, CD29 and its ligand, CD30 and its ligand, CD40 and its ligand gp39, CD44, CD45 and isoforms, CDw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1 and TCR

histocompatibility antigens, MHC class I or II, the Lewis Y antigens, SLex, SLey, SLea, and SLeb;

integrins, VLA-1, VLA-2, VLA-3, VLA-4, VLA-5, VLA-6, and LFA-1;

adhesion molecules, Mac-1 and p150,95;

selectins, L-selectin, P-selectin, and E-selectin and their counterreceptors VCAM-1, ICAM-1, ICAM-2, and LFA-3;

interleukins, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-11, IL-12, IL-13, IL-14, and IL-15;

interleukin receptors, IL-1R, IL-2R, IL-4R, IL-5R, IL-6R, IL-7R, IL-8R, IL-10R, IL-11R, IL-12R, IL-13R, IL-14R, and IL-15R;

chemokines, PF4, RANTES, MIP1α, MCP1, NAP-2, Groα, Groβ, and IL-8;

growth factors, TNFalpha, TGFbeta, TSH, VEGF/VPF, PTHrP, EGF family, FGF, PDGF family, endothelin, and gastrin releasing peptide (GRP);

growth factor receptors, TNFalphaR, RGFbetaR, TSHR, VEGFR/VPFR, FGFR, EGFR, PTHrPR, PDGFR family, EPO-R, GCSF-R and other hematopoietic receptors;

integrin receptors, IFNαR, IFNβR, and IFNγR;

Igs and their receptors, IgE, FceRI, and FCeRII;

tumor antigens, her2-neu, mucin, CEA and endosialin;

allergens, house dust mite antigen, lol p1 (grass) antigens, and urushiol;

viral proteins, CMV glycoproteins B, H, and gCIII, HIV-1 envelope glycoproteins, RSV envelope glycoproteins, HSV envelope glycoproteins, EBV envelope glycoproteins, VZV envelope glycoproteins, HPV envelope glycoproteins, Hepatitis family surface antigens;

toxins, pseudomonas endotoxin and osteopontin/uropontin, snake venom, and bee venom;

blood factors, complement C3b, complement C5a, complement C5b-9, Rh factor, fibrinogen, fibrin, and myelin associated growth inhibitor;

enzymes, cholesterol ester transfer protein, membrane bound matrix metalloproteases, and glutamic acid decarboxylase (GAD); and

miscellaneous antigens, ganglioside GD3, ganglioside GM2, LMP1, LMP2, eosinophil major basic protein, eosinophil cationic protein, pANCA, Amadori protein, Type IV collagen, glycated lipids, γ-interferon, A7, P-glycoprotein and Fas (AFO-1) and oxidized-LDL

which method comprises culturing the cell or cell line of claim 23 under conditions wherein said nucleotide sequence is expressed to produce said immunoglobulin or analog; and
recovering the immunoglobulin or analog.

25. Canceled

26. (Original) A antibody containing a fully human variable region or analog thereof which is specifically immunoreactive with an antigen selected from the group consisting of human IL-6, human IL-8, human TNFα, human CD4, human L-selectin, human gp39 and tetanus toxin C(TTC).

27. Canceled

28. Canceled

29. Canceled

30. Canceled

31. Canceled

32. Canceled

33. Canceled

34. (Original) The analog of claim 26 which is a single chain F_v.

35. (Original) A recombinant DNA molecule encoding the antibody or analog of claim 26.

36. (Original) A recombinant DNA molecule which comprises an expression system for the production of the antibody or analog of claim 26 which expression system comprises a nucleotide sequence encoding said antibody or analog operably linked to control sequences capable of effecting its expression.

37. (Original) A recombinant host cell which is modified to contain the DNA molecule of claim 36.

38. (Original) A method to produce an antibody or analog immunospecific for an antigen selected from the group consisting of human IL-6, human IL-8, human TNFα, human CD4, human L-selectin, human gp39 and tetanus toxin C(TTC), which method comprises culturing the cells of claim 37 under conditions wherein said coding sequence is expressed; and recovering the antibody or analog produced.

39 (Original) Use of the antibody or analog of claim 27, 29, 31 or 32 for treating an autoimmune disease in a mammal.

40. Canceled

41. Canceled

42. Canceled

43. Canceled

44. Canceled

45. Canceled

46. (New) An isolated human antibody or an antigen-binding fragment thereof that specifically binds a leukocyte marker selected from the group consisting of CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a, b, c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27, CD28, CD29, CD30, CD40, CD44, CD45 and isoforms, Cdw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1, and TCR,

wherein said antibody or fragment modulates the activity of said leukocyte marker.

47. (New) The antibody or fragment according to claim 46 wherein the leukocyte marker is CD4.

48. (New) The antibody or fragment according to claim 46 herein the leukocyte marker is CD8.

49. (New) The antibody or fragment according to claim 46 wherein the leukocyte marker is CD28.

50. (New) The antibody or fragment according to claim 46 wherein the leukocyte marker is CD40.

51. (New) The antibody or fragment according to claim 46 wherein the leukocyte marker is CD45.

52. (New) The antibody or fragment according to claim 46 wherein the leukocyte marker is TCR.

53. (New) The antibody according to any one of claims 46-52, wherein the antibody is monoclonal.

54. (New) The fragment according to any one of claims 46-52, wherein the fragment comprises an scFv, Fab, Fab', or $F(ab')_2$ fragment.

55. (New) The antibody according to any one of claims 46-52, wherein the antibody is detectably labeled.

56. (New) The antibody according to any one of claims 46-52, wherein the leukocyte marker is human.

57. (New) The antibody according to any one of claims 46-52, wherein the antibody decreases activity of the leukocyte marker.

58. (New) The antibody according to any one of claims 46-52, wherein the antibody comprises lambda light chain sequence.

59. (New) The antibody according to any one of claims 46-52, wherein the antibody increases an activity of the leukocyte marker.

60. (New) The antibody according to any one of claims 46-52, further comprising a pharmaceutical formulation.

61. (New) A host cell that expresses the antibody according to any one of claims 46-52.

62. (New) A nucleic acid that encodes the antibody according to any one of claims 46-52.

63. (New) A host cell comprising the nucleic acid of claim 62.

64. (New) A method of producing an isolated human antibody that specifically binds and modulates the activity of a leukocyte marker selected from the group consisting of CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a, b, c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27, CD28, CD29, CD30, CD40, CD44, CD45 and isoforms, Cdw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1, and TCR comprising:

(a) administering the leukocyte marker or an immunogenic fragment thereof to a mouse capable of expressing human immunoglobulin;

(b) screening the administered mouse for expression of a human antibody that specifically binds to the leukocyte marker;

(c) selecting a mouse that produces a human antibody that specifically binds to the leukocyte marker;

(d) isolating an antibody from the mouse that produces a human antibody that specifically binds to the leukocyte marker; and

(e) determining whether the antibody modulates an activity of the leukocyte marker thereby producing a human antibody that specifically binds to the leukocyte marker and modulates an activity of the leukocyte marker.

65. (New) A method of producing an isolated human antibody that specifically binds to and modulates the activity of a leukocyte marker selected from the group consisting of CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a, b, c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27, CD28, CD29, CD30, CD40, CD44, CD45 and isoforms, Cdw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1, and TCR comprising:

(a) administering the leukocyte marker or an immunogenic fragment thereof to a mouse capable of expressing human immunoglobulin;

(b) isolating spleen cells from the mouse that produces a human antibody that specifically binds to the leukocyte marker;

(c) fusing the spleen cells with a myeloma cell to produce a hybridoma; and

(d) screening the hybridoma for expression of a human antibody that specifically binds to and modulates an activity of the leukocyte marker thereby producing a human monoclonal antibody that specifically binds to and modulates an activity of the leukocyte marker.

66. (New) The method according to claim 64 or 65 wherein the leukocyte marker is CD4.

67. (New) The method according to claim 64 or 65 wherein the leukocyte marker is CD8.

68. (New) The method according to claim 64 or 65 wherein the leukocyte marker is CD28.

69. (New) The method according to claim 64 or 65 wherein the leukocyte marker is CD40.

70. (New) The method according to claim 64 or 65 wherein the leukocyte marker is CD45.

71. (New) The method according to claim 64 or 65 wherein the leukocyte marker is TCR.

72. (New) A monoclonal antibody isolated from a hybridoma produced by the method of claim 65.

73. (New) A method for modulating an activity of a leukocyte marker selected from the group consisting of CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a, b, c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27, CD28, CD29, CD30, CD40, CD44, CD45 and isoforms, Cdw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1, and TCR comprising contacting a cell that expresses the leukocyte marker with a modulating amount of the antibody of claim 46.

74. (New) The method according to claim 73 wherein the leukocyte marker is CD4.

75. (New) The method according to claim 73 wherein the leukocyte marker is CD8.

76. (New) The method according to claim 73 wherein the leukocyte marker is CD28.

77. (New) The method according to claim 73 wherein the leukocyte marker is CD40.

78. (New) The method according to claim 73 wherein the leukocyte marker is CD45.

79. (New) The method according to claim 73 wherein the leukocyte marker is TCR.

80. (New) The method of claim 73, wherein the leukocyte marker is human.

81. (New) The method of claim 73, wherein the activity is increased.

82. (New) The method of claim 73, wherein the activity is decreased.

83. (New) A method of increasing an activity of a leukocyte marker selected from the group consisting of CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a, b, c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27, CD28, CD29, CD30, CD40, CD44, CD45 and isoforms, Cdw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1, and TCR in a subject comprising administering to the subject an amount of a human antibody that increases an activity of the leukocyte marker.

84. (New) A method of decreasing an activity of a leukocyte marker selected from the group consisting of CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a, b, c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27, CD28, CD29, CD30, CD40, CD44, CD45 and isoforms, Cdw52 (Campath antigen), CD56,

CD58, CD69, CD72, CTLA-4, LFA-1, and TCR in a subject comprising administering to the subject an amount of a human antibody that decreases an activity of the leukocyte marker.

85. (New) A method of detecting the presence of a leukocyte marker selected from the group consisting of CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a, b, c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27, CD28, CD29, CD30, CD40, CD44, CD45 and isoforms, Cdw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1, and TCR in a sample or a cell, comprising contacting a sample having or suspected of having the leukocyte marker, or a cell expressing or suspected of expressing the leukocyte marker, with the antibody of claim 1, and detecting the presence of the leukocyte marker in the sample or cell.

86. (New) The method according to claim 83, 84 or 85, wherein the leukocyte marker is CD4.

87. (New) The method according to claim 83, 84 or 85, wherein the leukocyte marker is CD8.

88. (New) The method according to claim 83, 84 or 85, wherein the leukocyte marker is CD28.

89. (New) The method according to claim 83, 84 or 85, wherein the leukocyte marker is CD40.

90. (New) The method according to claim 83, 84 or 85, wherein the leukocyte marker is CD45.

91. (New) The method according to claim 83, 84 or 85, wherein the leukocyte marker is TCR.

92. (New) The method of claim 85, wherein the cell is in a subject.

93. (New) A method of detecting the presence of a disorder associated with increased or decreased expression of a a leukocyte marker selected from the group consisting of CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a, b, c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27, CD28, CD29, CD30, CD40, CD44, CD45 and isoforms, Cdw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1, and TCR in a human, comprising contacting a sample having or suspected of having the leukocyte marker or a cell expressing or suspected of expressing the leukocyte marker, wherein the sample or cell is from or present in the human, with the human antibody of claim 46 and detecting the presence of increased or decreased expression of the leukocte marker in the sample or cell relative to a control thereby detecting

the presence of a disorder associated with increased or decreased expression of the leukocyte marker in the human.

94. (New) The method according to claim 93, wherein the leukocyte marker is CD4.

95. (New) The method according to claim 93, wherein the leukocyte marker is CD8.

96. (New) The method according to claim 93, wherein the leukocyte marker is CD28.

97. (New) The method according to claim 93, wherein the leukocyte marker is CD40.

98. (New) The method according to claim 93, wherein the leukocyte marker is CD45.

99. (New) The method according to claim 93, wherein the leukocyte marker is TCR.